Claims

We claim:

1. A mosaic protein comprising a plurality of homologous antigenic peptides from different genotypes of a species.

2. The mosaic protein of Claim 1, wherein the species is a hepatitis virus.

3. The mosaic protein of Claim 2, wherein the hepatitis virus is a hepatitis C virus.

4. The mosaic protein of Claim 3, wherein the antigenic peptides are from nucleocapsid proteins.

5. The mosaic protein of Claim 4, comprising the amino acid sequences set forth in SEQ ID NOs:23-33.

6. A method of detecting a hepatitis infection in an individual comprising combining a serum sample from the individual with the mosaic protein of Claim 2, and detecting the presence of antibody binding to the mosaic protein, the presence of binding indicating a hepatitis infection in the individual.

7. The method of Claim 6, wherein the antigenic peptides are from nucleocapsid proteins.

8. The method of Claim 7, wherein the mosaic protein comprises the amino acid sequences set forth in SEQ ID NOs:23-33.

9. The mosaic protein of Claim 3, wherein the antigenic peptides are from non-structural proteins.

10. The mosaic protein of Claim 9, comprising the amino acid sequence set forth in SEQ ID NO:52.

11. The method of Claim 6, wherein the antigenic peptides are from non-structural proteins.

12. The method of Claim 11, wherein the mosaic protein comprises the amino acid sequence set forth in SEQ ID NO:52.

13. A nucleic acid encoding a mosaic protein, wherein the mosaic protein comprises a plurality of homologous antigenic peptides from different genotypes of a species.

14. The nucleic acid of Claim 13, wherein the species is a hepatitis virus.

15. The nucleic acid of Claim 14, wherein the hepatitis virus is a hepatitis C virus.

16. The nucleic acid of Claim 15, wherein the antigenic peptides are from nucleocapsid proteins.

17. The nucleic acid of Claim 16, wherein the mosaic protein comprises the amino acid sequences set forth in SEQ ID NOs:23-33.

18. The nucleic acid of Claim 15, wherein the antigenic peptides are from non-structural proteins.

19. The nucleic acid of Claim 18, wherein the mosaic protein comprises the amino acid sequence set forth in SEQ ID NO:52.

20.   A method of constructing an artificial gene, comprising:

a.   synthesizing an initial oligonucleotide containing an initial gene segment encoding an initial gene product,

wherein the initial gene segment is flanked in the upstream direction by an upstream initial ligating sequence, a first endonuclease recognition sequence that is recognized by a first endonuclease that cleaves at the first endonuclease recognition sequence, and a second endonuclease recognition sequence which is recognized by a second endonuclease that cleaves downstream of the first endonuclease recognition sequence and within the upstream initial ligating sequence,

and wherein the initial gene segment is flanked in the downstream direction by a downstream initial ligating sequence, a stop codon, a third endonuclease recognition sequence that is recognized by a third endonuclease that cleaves at the third endonuclease recognition sequence, and a fourth endonuclease recognition sequence which is recognized by a fourth endonuclease that cleaves upstream of the third endonuclease recognition sequence, upstream of the stop codon, and within the downstream initial ligating sequence;

b.   synthesizing a subsequent oligonucleotide containing a subsequent gene segment encoding a subsequent gene product,

wherein the subsequent gene segment is flanked in the upstream direction by an upstream subsequent ligating sequence, a first endonuclease recognition sequence which is recognized by the first endonuclease that cleaves at the first endonuclease recognition sequence, and a second endonuclease recognition sequence which is recognized by the second endonuclease that cleaves downstream of the first endonuclease recognition sequence and within the upstream subsequent ligating sequence,

and wherein the subsequent gene segment is flanked in the downstream direction by a downstream subsequent ligating sequence, a stop codon, a third endonuclease recognition sequence which is recognized by the third endonuclease that cleaves at the third endonuclease recognition sequence, and a fourth endonuclease recognition sequence which is recognized by

the fourth endonuclease that cleaves upstream of the third endonuclease recognition sequence, upstream of the stop codon, and within the downstream subsequent ligating sequence;

    c.   cleaving the initial oligonucleotide with the fourth endonuclease, and cleaving the subsequent oligonucleotide with the second endonuclease; and

    d.   ligating the initial oligonucleotide and the subsequent oligonucleotide together at the downstream initial ligating sequence of the initial oligonucleotide and the upstream subsequent ligating sequence of the subsequent oligonucleotide to form an artificial gene.

21.   The method of Claim 20, further comprising the subsequent step of cleaving the artificial gene with the first and third endonucleases and inserting the remaining artificial gene into a vector previously cleaved with the first and third endonucleases.

22.   The method of Claim 20, further comprising following the synthesizing the initial oligonucleotide step, and before the cleaving the initial oligonucleotide with the fourth endonuclease step, the additional step of:

    confirming the operability of the initial oligonucleotide by cleaving the initial oligonucleotide with the first and third endonucleases and inserting the remaining initial oligonucleotide into a vector previously cleaved with the first and third endonucleases, and expressing the initial gene segment.

23.   The method of Claim 20, wherein the first endonuclease is EcoRI, the second endonuclease is BbvI, the third endonuclease is BamHI, or the fourth endonuclease is FokI.

24.   The method of Claim 20, wherein the gene segments encode antigenic regions of different genotypes of a hepatitis virus.

25.   The method of Claim 20, wherein the gene segments encode antigenic regions of different genotypes of a hepatitis C virus.

26. The method of Claim 20, wherein the gene segments encode antigenic regions of a nucleocapsid protein or a non-structural protein of different genotypes of a hepatitis C virus.

27. An artificial gene constructed by the method of Claim 20.

28. A mosaic protein encoded by the artificial gene constructed by the method of Claim 20.

29. The mosaic protein of Claim 28, wherein the gene segments encode antigenic regions of different genotypes of a hepatitis virus.

30. A method of detecting a hepatitis infection in an individual comprising combining a serum sample from the individual with the mosaic protein of Claim 29, and detecting the presence of antibody binding to the mosaic protein, the presence of binding indicating a hepatitis infection in the individual.

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